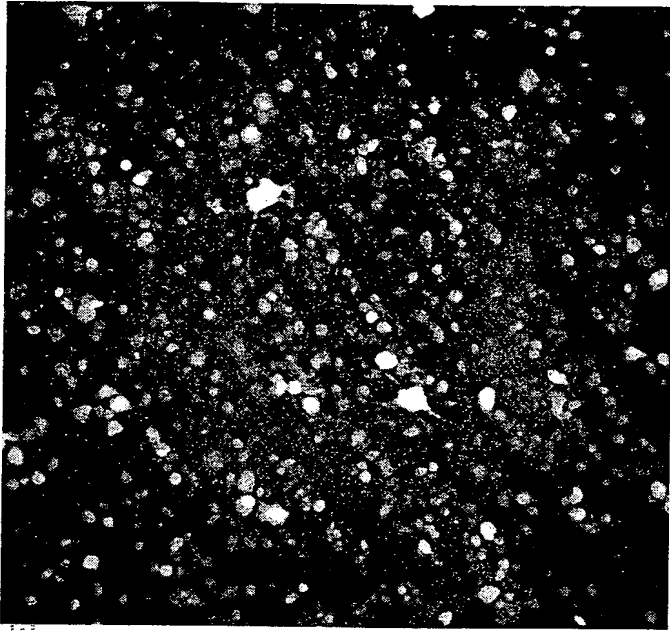
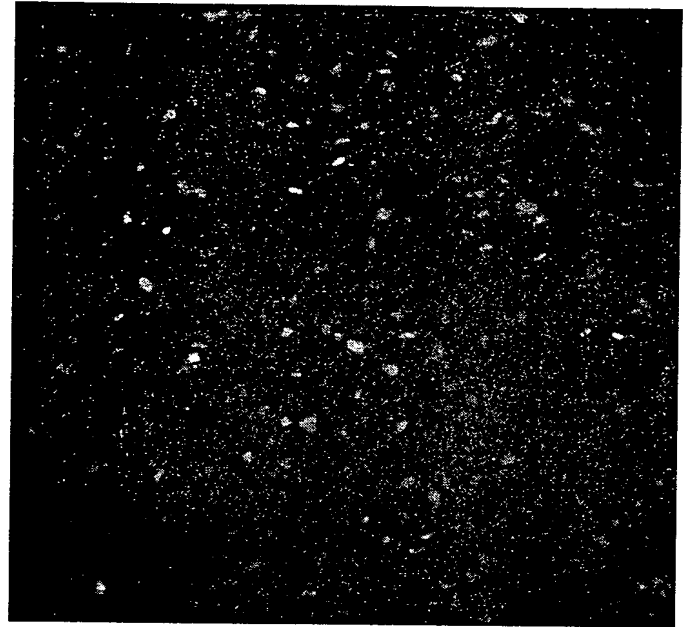


Figure 1

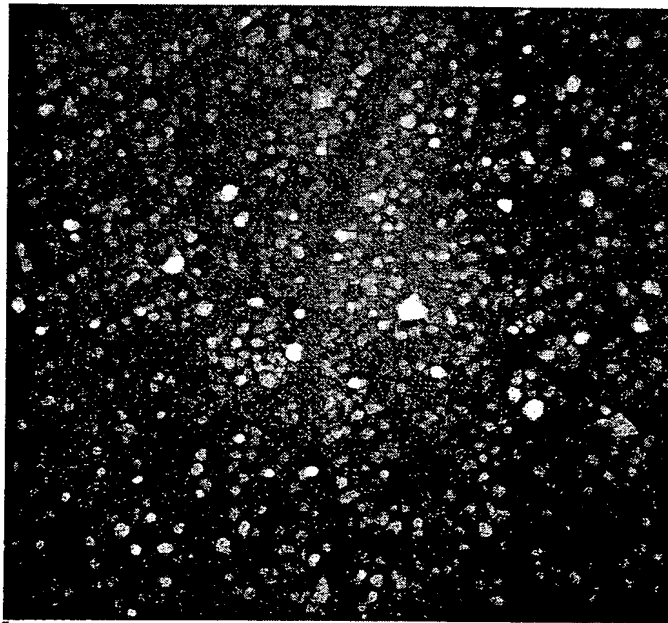
GPI 1046 protects ganglion cells against degeneration due to 1 hour of retinal ischemia
Fluorogold labelled retinal ganglion cells in wholemount, 28 days after ischemic episode



A. Labelled retinal ganglion cells in the
Normal central retina



B. 1 hour of retinal ischemia produces
extensive loss of ganglion cells

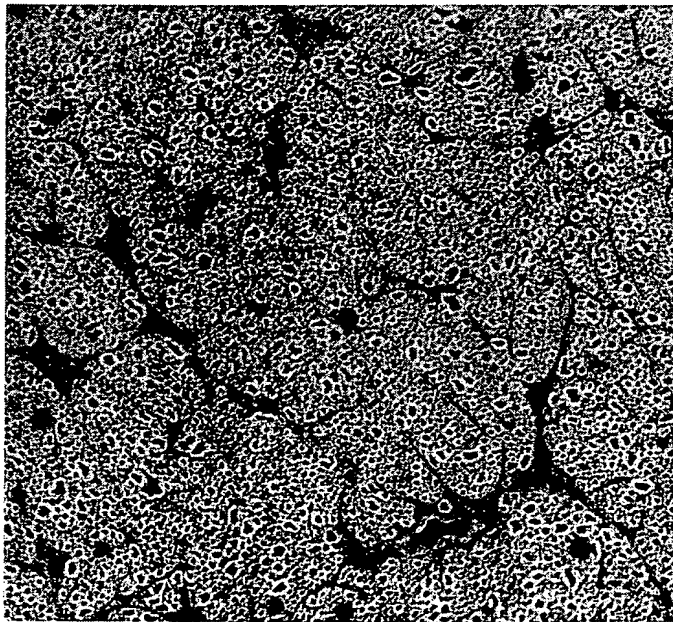


C. Administration of GPI 1046 1 hour before retinal ischemia
and for 4 days subsequently produces significant protection of vulnerable retinal ganglion cells

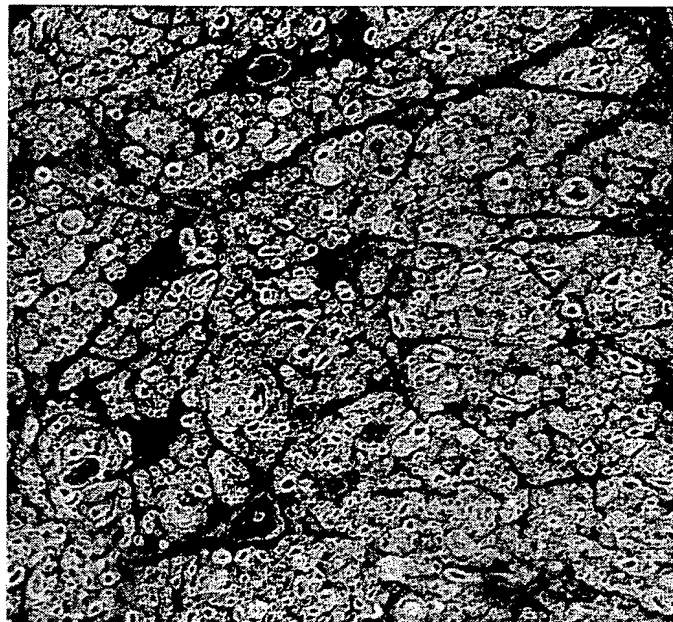
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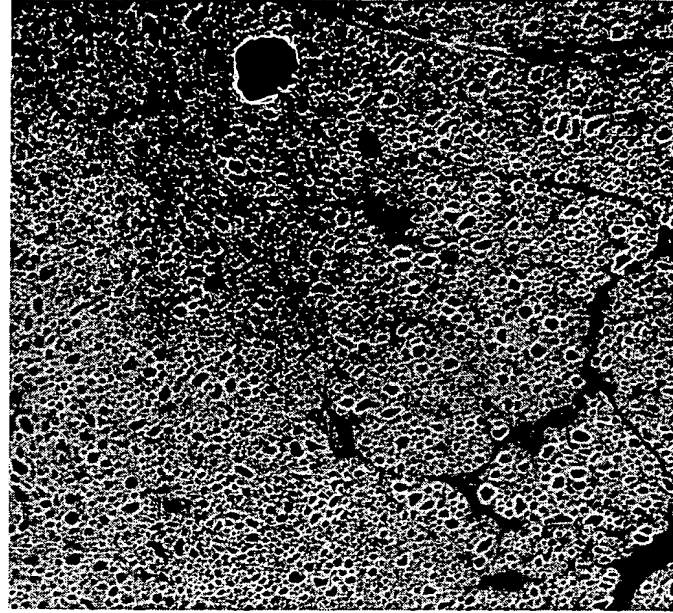
Figure 2
GPI 1046 Protects retinal ganglion cell axons and prevents myelin degeneration
in the optic nerve induced by 1 hour of complete retinal ischemia,
toluidine blue stained optic nerve cross sections, 630X



A. Normal optic nerve

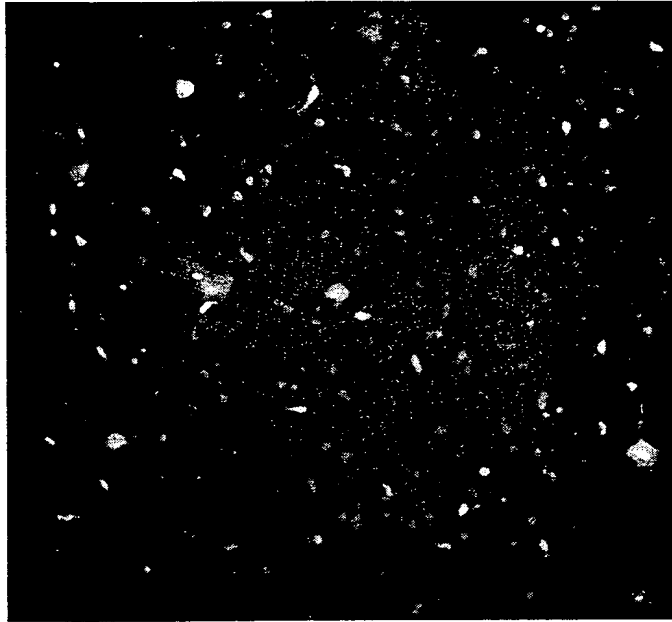


B. Vehicle treated optic nerve 28 days
after 1 hour complete retinal ischemia



C. GPI 1046 treated optic nerve 28 days
after 1 hour complete retinal ischemia

**GPI 1046 administration for 28 days
provides only moderate protection of
axotomized retinal ganglion cells**



Florogold labelled RGCs 90 days following transection,
Treatment with vehicle alone for 1st 28 days

Florogold labelled RGCs 90 days following transection,
Treatment with GPI 1046 for 1st 28 days
Treatment with vehicle alone for 1st 28 days

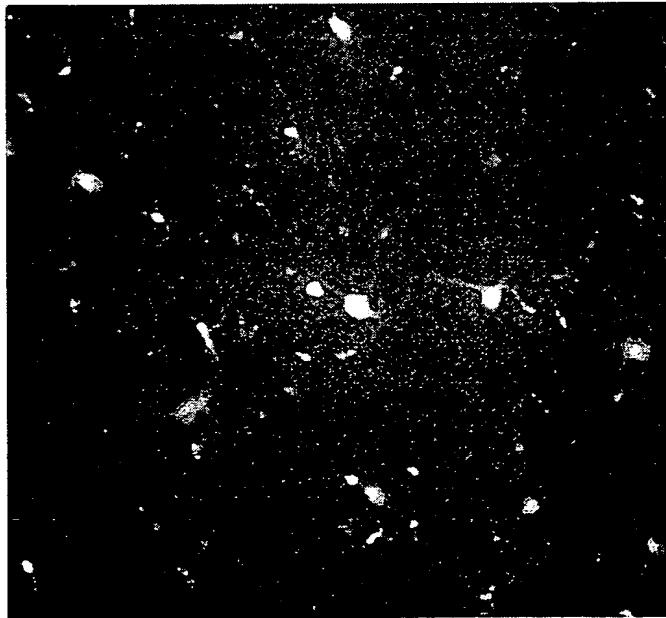
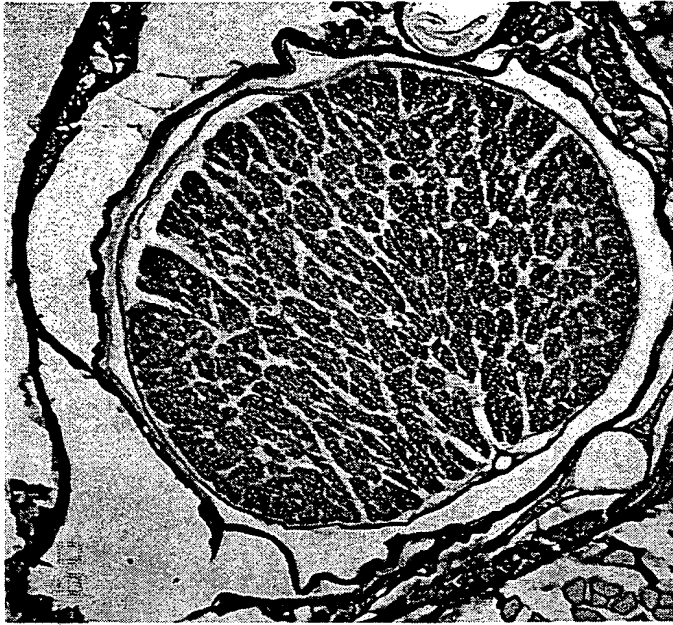


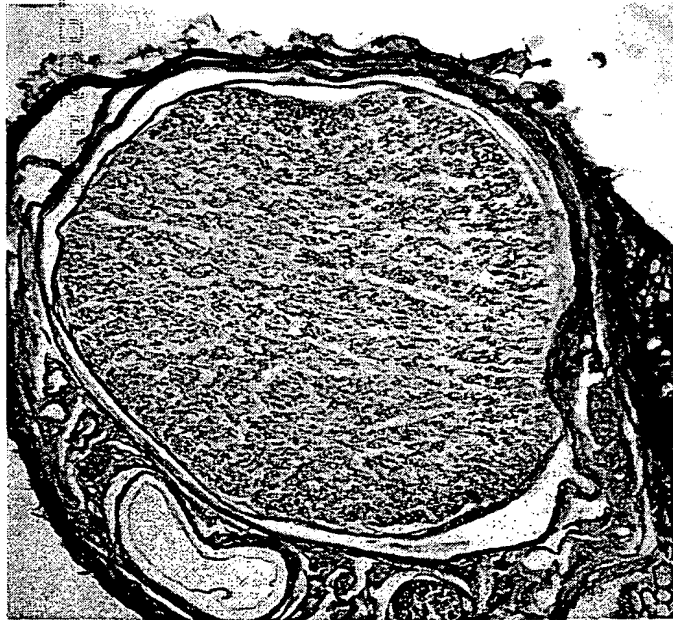
Figure 4
GPI 1046 prevents axonal degeneration in the proximal stump of the optic nerve
RT97 neurofilament immunohistochemistry,
optic nerve cross sections, 90 days after complete transection



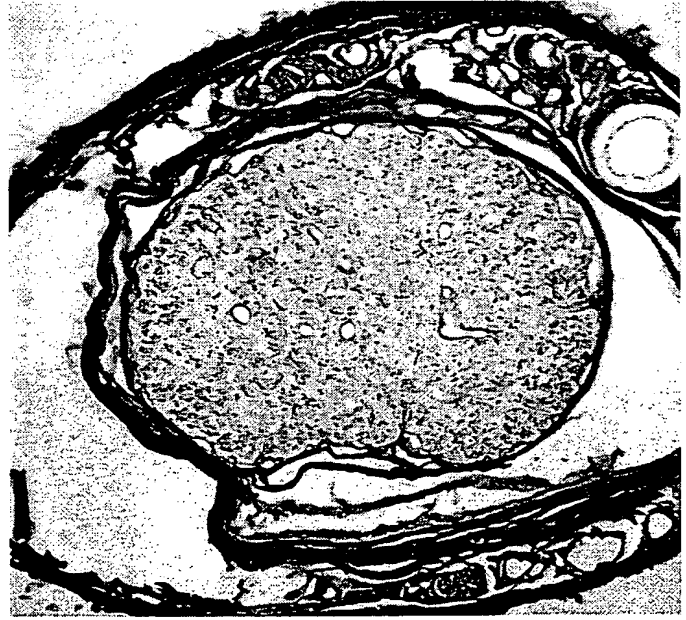
A. Sham



B. Optic nerve transection (ONT) 90 days survival



**C. optic nerve 90 days after transection,
GPI 1046 treatment days 1-28**

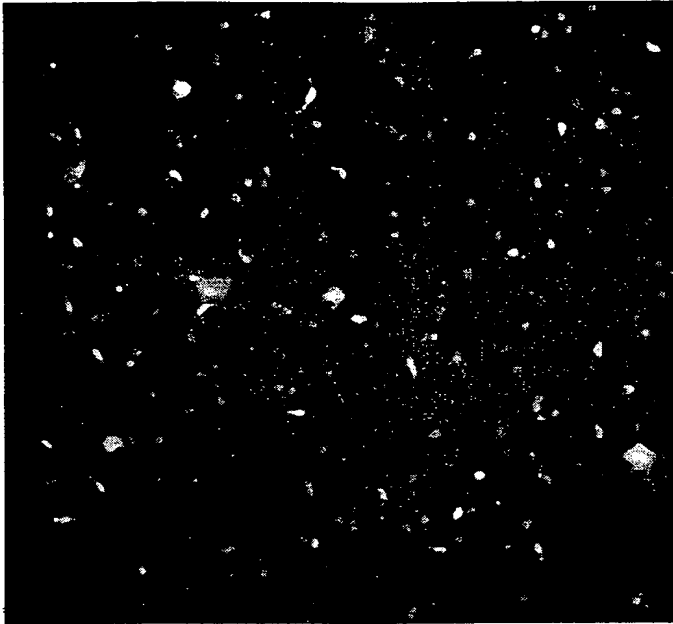


**D. optic nerve 90 days after transection,
GPI 1046 treatment days 1-14**

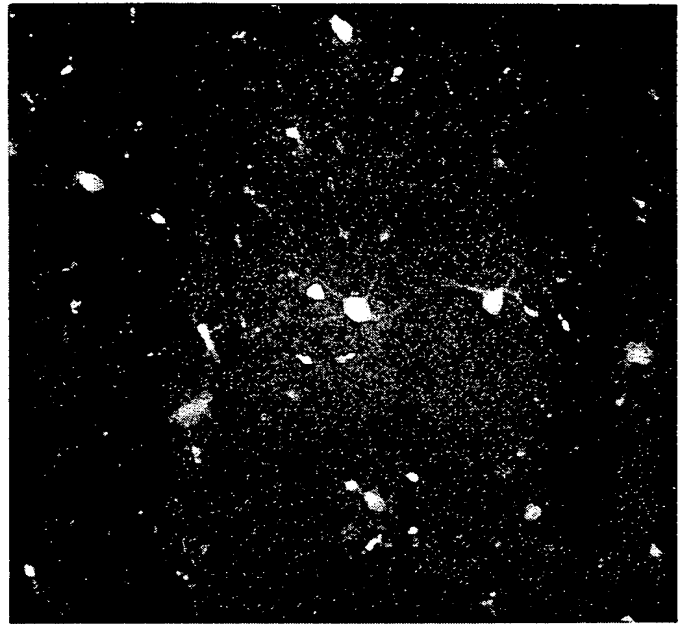
Figure 5

**GPI 1046 administration for 28 days provides only moderate protection
of axotomized retinal ganglion cells**

Fluorogold labelled retinal ganglion cells 90 days following transection



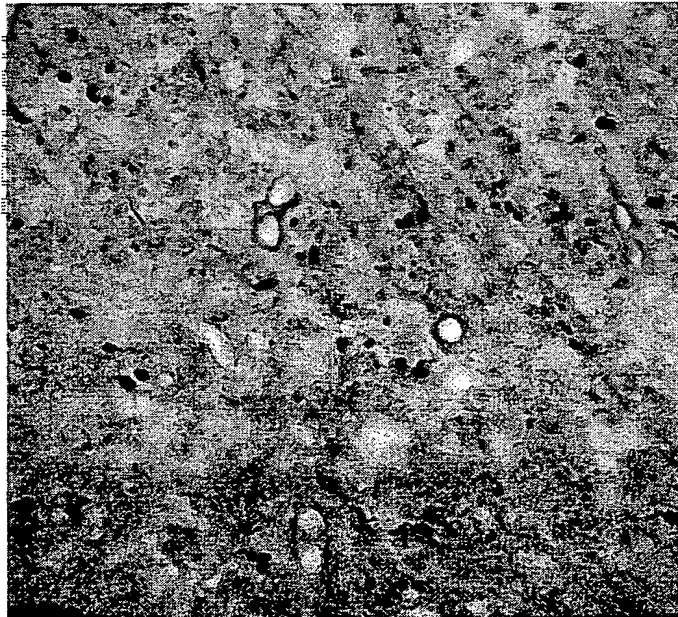
vehicle administered for 1st 28 days



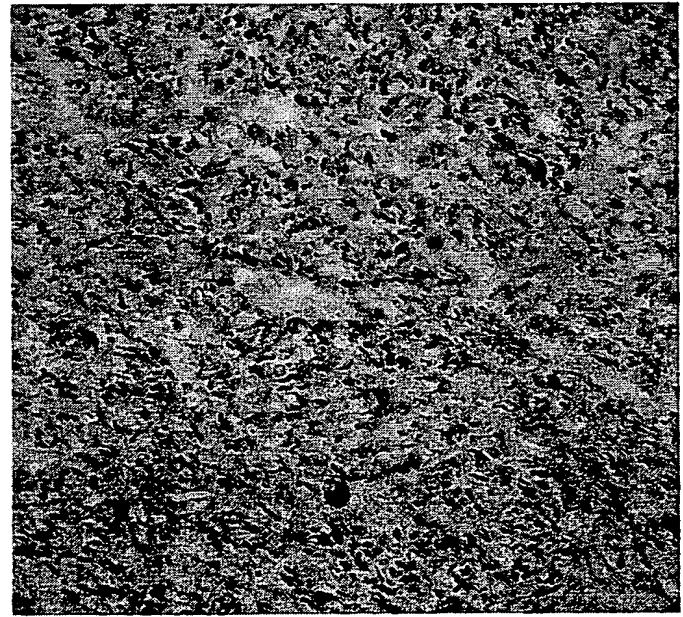
GPI 1046 administered for 1st 28 days

**GPI 1046 administration for 28 days preserves optic nerve axons
of surviving retinal ganglion cells**

RT 97 neurofilament immunohistochemistry 90 days after transection



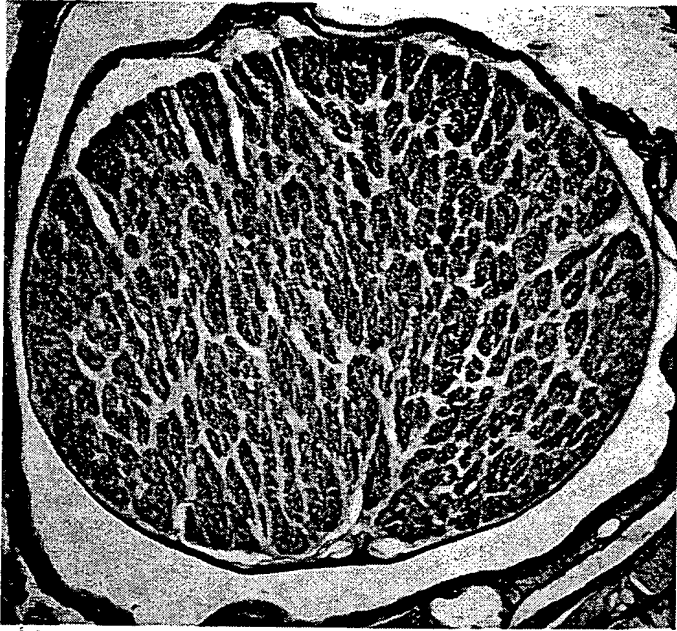
vehicle administered for 1st 28 days



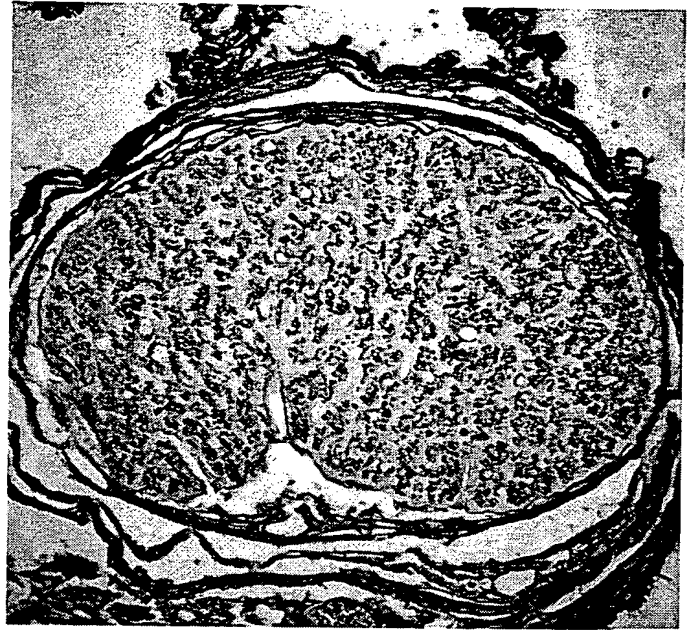
GPI 1046 administered for 1st 28 days

Figure 6

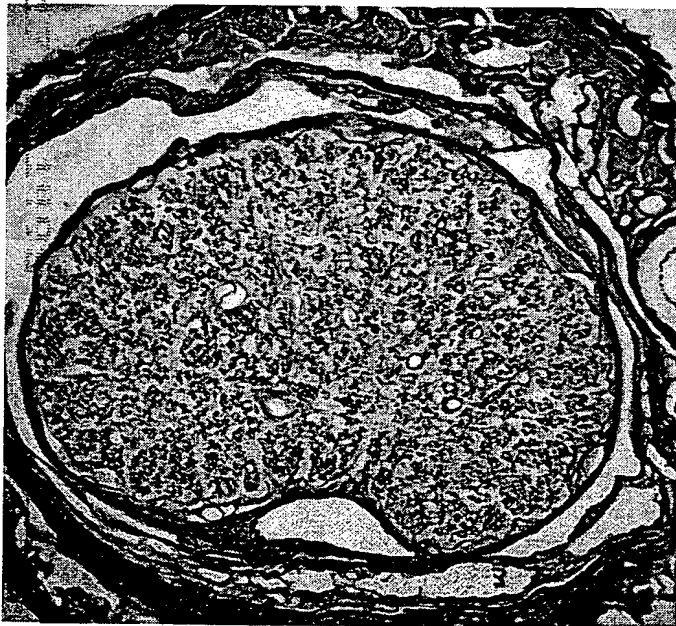
**Preservation of myelin in the proximal stump of the optic nerve 90 days after transection
14 vs 28 days treatment with GPI 1046 10mg/kg s.c.**



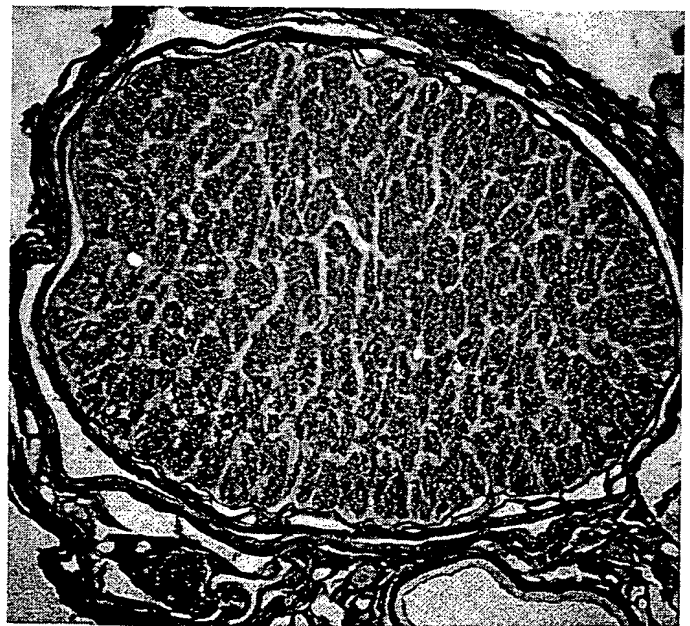
Normal(sham) Optic nerve



90 days after optic nerve transection, vehicle treated



90 days after optic nerve transection, 14 days GPI 1046



90 days after optic nerve transection, 28 days GPI 1046

myelin basic protein immunohistochemistry (SMI-94), 20X

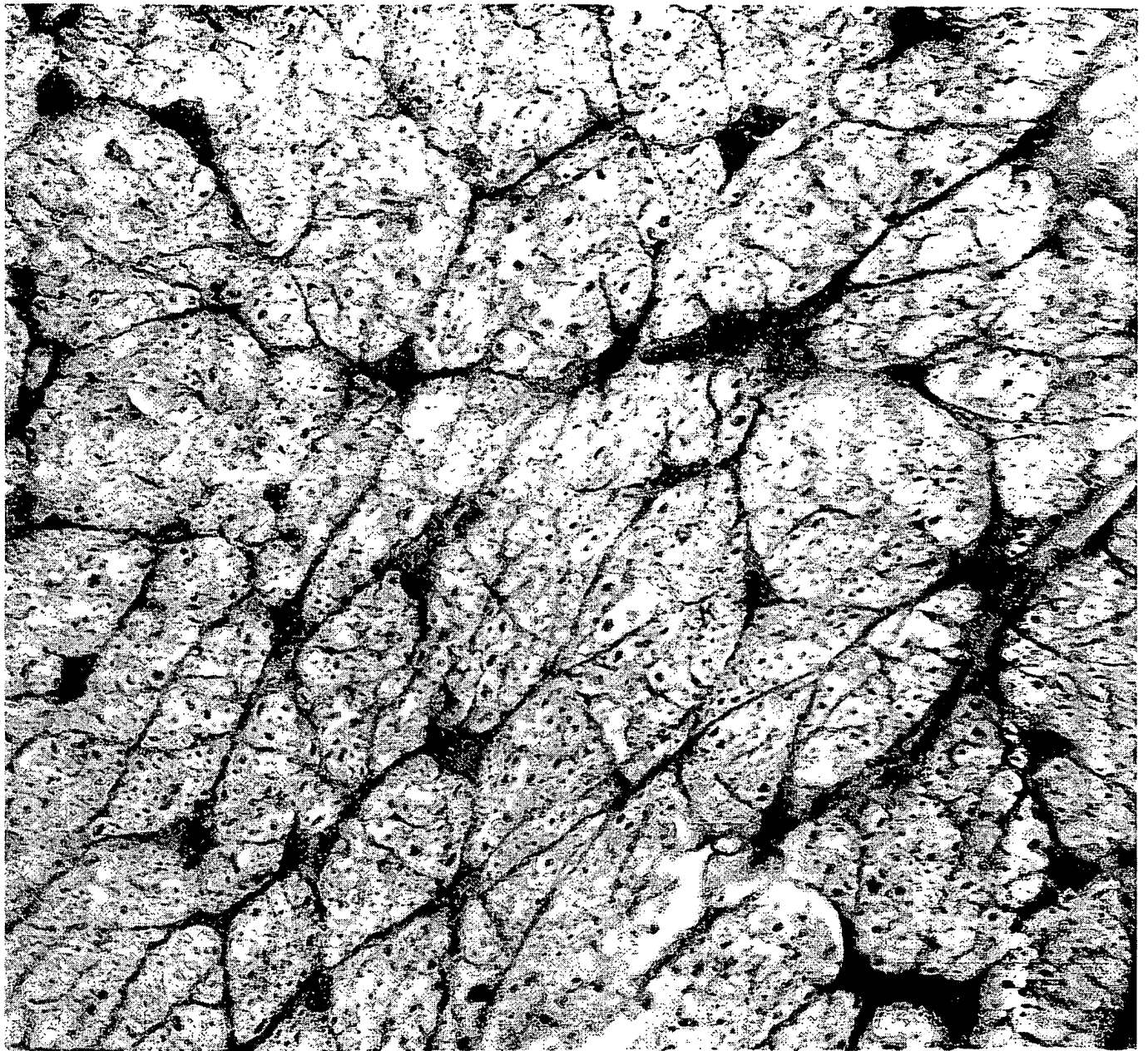
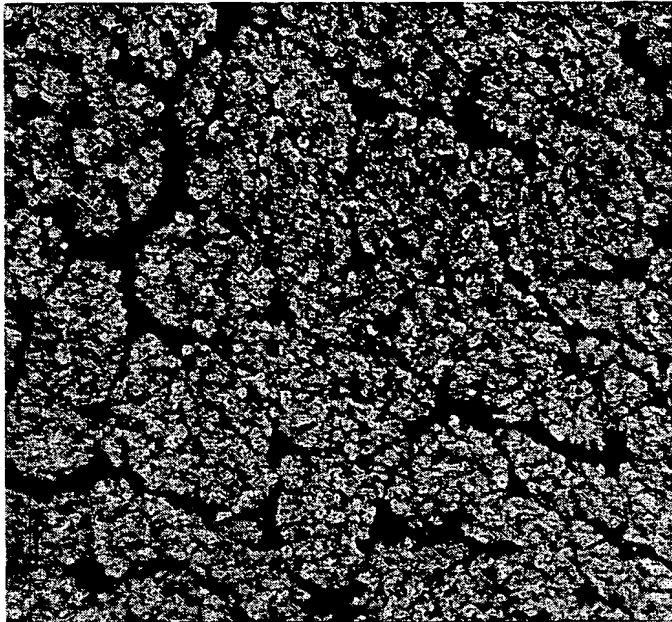
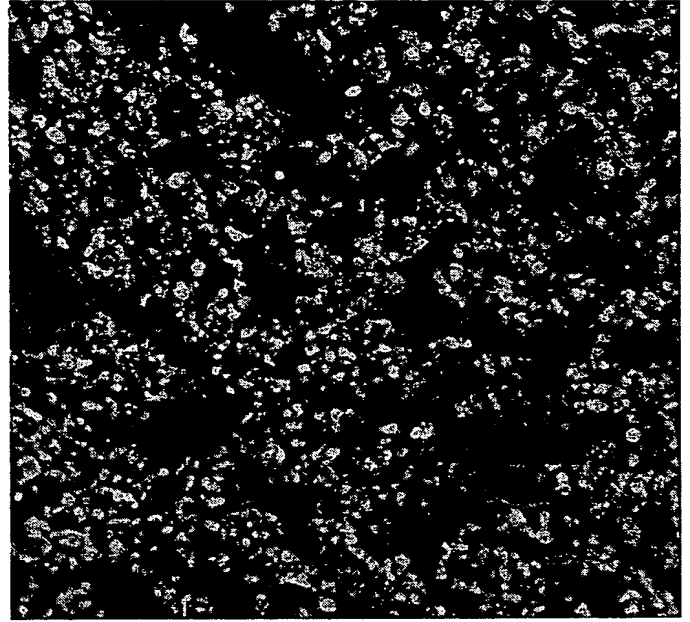


Figure 7
FKBP-12 immunohistochemistry labels oligodendroglia and axons in the normal optic nerve

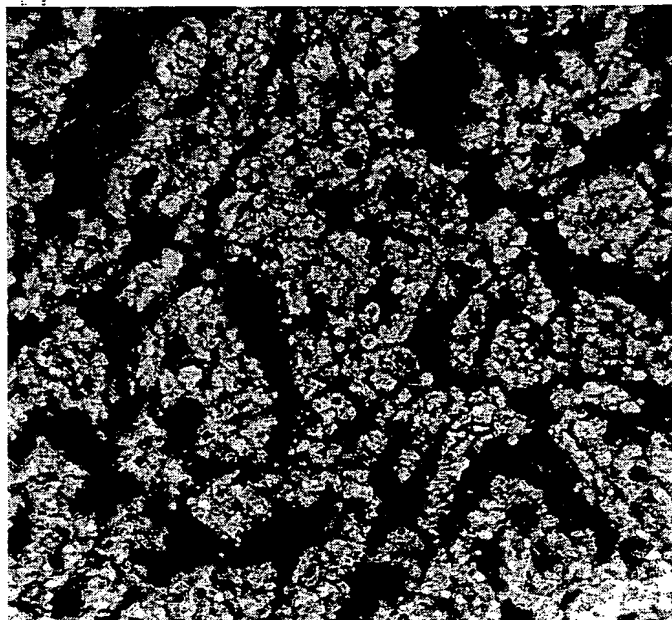
**GPI 1046 treatment prevents myelin degeneration
in the distal stump of the optic nerve
Myelin basic protein immunohistochemistry 90 days after transection**



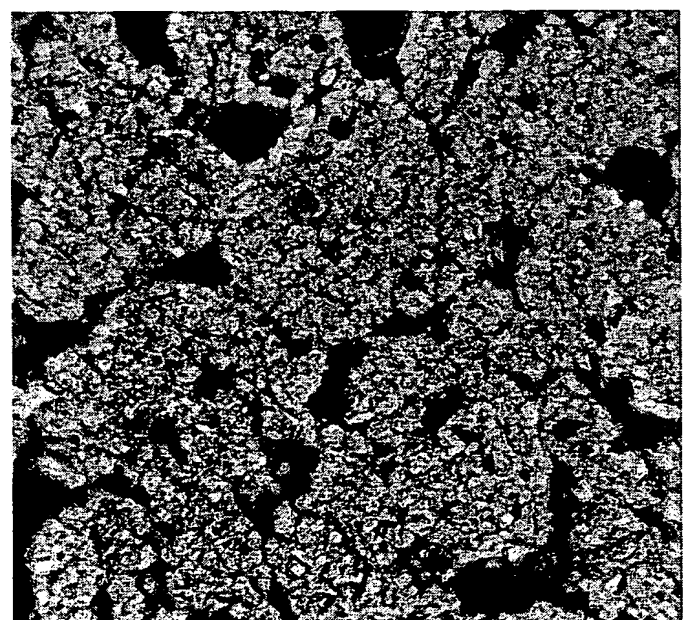
A. Normal optic nerve



**B. Distal optic nerve stump
90 days after complete transection**



**C. Distal optic nerve stump
90 days after complete transection
GPI 1046 administered 1-14 days
after transection**



**D. Distal optic nerve stump
90 days after complete transection
GPI 1046 administered 1-28 days
after transection**

Figure 9

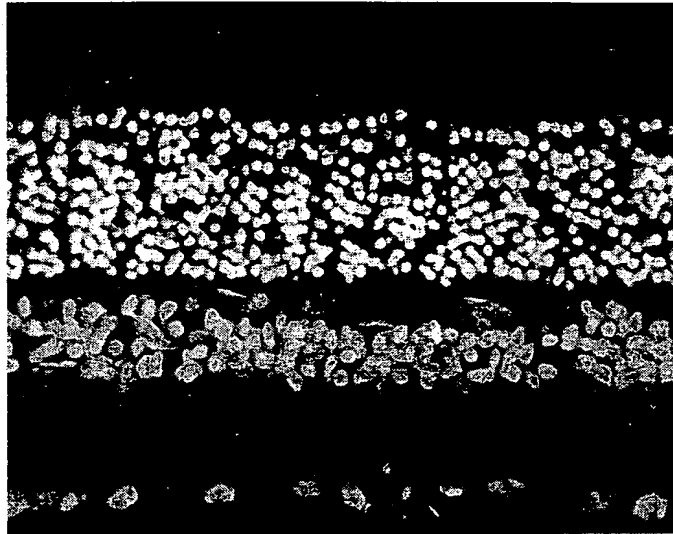
GPI 1046 decreases neovascularization and prevents neuronal loss in the inner retinal in the Streptozotocin model of diabetic retinopathy

**A. Normal
retina
Cross section
Cresyl violet**

**Outer Nuclear
layer (ONL)**

**Inner Nuclear
layer (INL)**

**Ganglion cell
layer (GCL)**

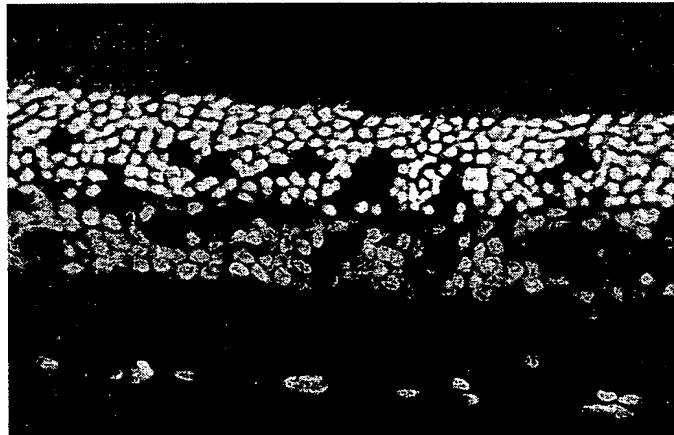


**B. retina from
Streptozotocin
/vehicle case**

ONL

INL

GCL

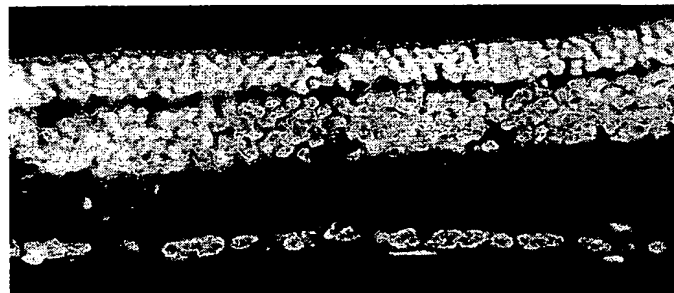


**C. Retina from
Streptozotocin
/GPI 1046 case**

ONL

INL

GCL



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